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Symbol / Name	Synonyms	Organism
PLK4 polo-like kinase 4	PLK-4, Polo-like kinase 4, Sak, SAK, Serine/threonine-protein kinase 18, Serine/threonine-protein kinase PLK4, Serine/threonine-protein kinase Sak, STK18	Homo sapiens

WikiGenes	edit this page new
UniProt	O00444, O15455, B7Z5G7
IntAct	O00444
PDB Structure	3COK
OMIM	605031
NCBI Gene	10733
NCBI RefSeq	NP_001177728, NP_055079
NCBI RefSeq	NM_014264, NM_001190801
NCBI UniGene	10733
NCBI Accession	Y13115, Z25433

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Collectively, our results suggest that CUL1 may **function** as a tumor suppressor by **regulating** PLK4 protein levels and thereby restraining excessive daughter centriole formation at maternal centrioles. [2009]

Plk4 trans-autophosphorylation **regulates** centriole number by controlling betaTrCP-mediated degradation. [2010]

Cep152 **interacts** with Plk4 [?] and is required for centriole duplication. [2010]

Cep152 can be **phosphorylated** by Plk4 [?] in vitro, suggesting that Cep152 acts with Plk4 [?] to initiate centriole formation. [2010]

Cullin 1 **functions** as a centrosomal suppressor of centriole multiplication by **regulating** polo-like kinase 4 protein levels. [2009]

Furthermore, our results imply that Plk2 **mediated** centriole duplication is dependent on Plk4 function. [2008]

Overexpression of a Plk4-**binding**-deficient mutant of Asl prevented centriole duplication in cultured cells and embryos. [2010]

Interfering with Cep152 **function** prevents recruitment of Plk4 to the centrosome and **promotes** loss of CPAP, a protein required for the control of centriole length in Plk4-regulated centriole biogenesis. [2010]

Our results suggest that Cep152 **recruits** Plk4 and CPAP to the centrosome to ensure a faithful centrosome duplication process. [2010]

In this study, we show in human and frog cells that Plk4 [?] **interacts** with the centrosome protein Cep152, the orthologue of Drosophila melanogaster Asterless. [2010]

Thus, SAK repression by p53 is likely **mediated** through the recruitment of HDAC repressors, and SAK repression contributes to p53-induced apoptosis. [2005]

We conclude that active Plk4 **promotes** its own degradation by catalyzing betaTrCP binding through trans-autophosphorylation (phosphorylation by the other kinase in the dimer) within homodimers. [2010]

Significantly, p53-**mediated** SAK repression was largely reversed in a dose-dependent manner by Trichostatin A [?], a potent histone deacetylase (HDAC) inhibitor, suggesting an involvement of HDAC transcription repressors in SAK repression by p53. [2005]

CONCLUSIONS: SAK [?]/PLK4 [?] is necessary for centriole duplication both in Drosophila and human cells. [2005]

Concept & Implementation by Robert Hoffmann

While significant advances have been made in understanding how PLK4 is regulated it is certain that additional regulatory mechanisms exist to safeguard the fidelity of centriole duplication. [2010]

PLK4 is required for centriole duplication and strongly stimulates centriole multiplication when aberrantly expressed. [2009]

We found that this activity of CUL1 involves the degradation of Polo-like kinase 4 (PLK4) at maternal centrioles. [2009]

The Polo kinase Plk4 functions in centriole duplication. [2005]

Here, we identify Plk4 as a key regulator of centriole duplication. [2005]

Finally, we show that depletion of SAK [?] in human cells also prevents centriole duplication and gives rise to mitotic abnormalities. [2005]

top

Unexpectedly, we found that stable overexpression of kinase-dead Plk4 leads to centriole overduplication. [2010]

Our data indicate that centriole overduplication results from disruption of Plk4 trans-autophosphorylation by kinase-dead Plk4, which then shields endogenous Plk4 from recognition by betaTrCP. [2010]

Autophosphorylation of polo-like kinase 4 and its role in centriole duplication. [2010]

Polo-like kinase 4 (PLK4) is a key regulator of this process whose kinase activity is essential for centriole duplication. [2010]

Depletion of Cep152 prevents both normal centriole duplication and Plk4 [?]-induced centriole amplification and results in a failure to localize Sas6 to the centriole, an early step in duplication. [2010]

Overexpression of Cep152 (1-217) mislocalizes Plk4 [?], but both Cep152 and Plk4 [?] are able to localize to the centriole independently of the other. [2010]

Our findings identify independent functions for Asl as a scaffold for Plk4 and Sas-4 that facilitates self-assembly and duplication of the centriole and organization of pericentriolar material. [2010]

Centriole assembly and duplication is controlled by Polo-like-kinase 4 (Plk4): these processes fail if Plk4 is downregulated and are promoted by Plk4 overexpression. [2010]

These data suggest that PLK4 activity is restricted to the centrosome to prevent aberrant centriole assembly and sustained kinase activity is required for centriole duplication. [2010]

Recent data have also shown that active PLK4 is restricted to the centrosome, a mechanism that could serve to prevent aberrant centriole assembly elsewhere in the cell. [2010]

We show that overexpression of Polo-like kinase 4 (Plk4) in human cells induces centrosome amplification through the simultaneous generation of multiple procentrioles adjoining each parental centriole. [2007]

Plk4-induced centriole biogenesis in human cells. [2007]

The centriolar protein Polo-like kinase 4 (Plk4) is a key regulator of centriole biogenesis and is crucial for maintaining constant centriole number, but the mechanisms regulating its activity and expression are only beginning to emerge. [2010]

Gamma-tubulin-containing abnormal centrioles are induced by insufficient Plk4 in human HCT116 colorectal cancer cells. [2009]

In this study, we show that the pericentriolar material protein, Cep152, interacts with the distinctive cryptic Polo-box of Plk4 via its N-terminal domain and is required for Plk4-induced centriole overduplication. [2010]

Activation of PLK4 at the replicating daughter centriole is delayed until G2, but a level equivalent to the replicating mother centriole is achieved in M phase. [2010]

Autophosphorylation probably plays a role in the process of centriole duplication, because mimicking S305 phosphorylation enhances the ability of overexpressed PLK4 to induce centriole amplification. [2010]

Cep152 and Plk4 [?] colocalize at the centriole throughout the cell cycle. [2010]

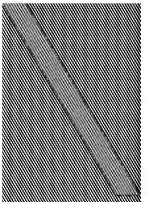
SAK [?]/PLK4 [?] is required for centriole duplication and flagella development. [2005]

These results suggest that HCT116 cells fail to organize the ninefold symmetry of centrioles due to insufficient Plk4. [2009]

top

Plk4, a mammalian homolog of ZYG-1 essential for initiation of centriole biogenesis, is not associated with the gamma-tubulin-specific abnormal centrosomes. [2009]

Both gain and loss of function studies have identified the Polo-like kinase Plk4/Sak as a crucial regulator of centriole biogenesis, but the mechanisms governing centrosome duplication are incompletely understood. [2010]



RESULTS: Here, we show that downregulation of SAK [?] in Drosophila cells, by mutation or RNAi, leads to loss of centrioles, the core structures of centrosomes. [2005]

Centrioles duplicate once per cell cycle, and duplication requires Plk4 [?], a member of the Polo-like kinase family; however, the mechanism linking Plk4 [?] activity and centriole formation is unknown. [2010]

Active PLK4 is detectable on the replicating mother centriole in G1/S [?], with the proportion of active kinase increasing through interphase to reach a maximum in mitosis. [2010]

The majority of spermatids in SAK [?] mutants lack centrioles and so are unable to make sperm axonemes. [2005]

We also show that SAK [?] mutants lose their centrioles during the mitotic divisions preceding male meiosis but still produce cysts of 16 primary spermatocytes as in the wild-type. [2005]

Importantly, we show that S305-phosphorylated PLK4 is specifically sequestered at the centrosome contrary to the nonphosphorylated form. [2010]

The amount of Plk4 at each centrosome was less in cells with abnormal centrosomes than cells without gamma-tubulin-specific abnormal centrosomes. [2009]

Cep152 acts as a scaffold for recruitment of Plk4 and CPAP to the centrosome. [2010]

Both gain- and loss-of-function experiments demonstrate that Plk4 is required--in cooperation with Cdk2, SPD2 and Hs-SAS6--for the precise reproduction of centrosomes during the cell cycle. [2005]

Comparative expression of the mitotic regulators SAK and PLK in colorectal cancer. [2001]

CONCLUSIONS: The polo family mitotic regulators SAK and PLK are both aberrantly expressed in colorectal cancer. [2001]

The potential prognostic significance of SAK and PLK expression in colorectal cancer will be evaluated in the future. [2001]

METHODS: In this study, SAK expression was evaluated in a series of sporadic human colorectal cancer specimens (n = 74) and compared with that of PLK. [2001]

The interaction requires the N-terminal 217 residues of Cep152 and the crypto Polo-box of Plk4 [?]. [2010]

Here we show that the centriolar protein Asterless (Asl; human orthologue CEP152) provides a conserved molecular platform, the amino terminus of which interacts with the cryptic Polo box of Plk4, whereas the carboxy terminus interacts with the centriolar protein Sas-4 (CPAP in humans). [2010]

Here, we show that PLK4 autophosphorylation of serine S305 is a consequence of kinase activation and enables the active fraction to be identified in the cell. [2010]

Human cells depleted of SAK [?] show error-prone mitosis, likely to underlie its tumor-suppressor role. [2005]

SAK, a new polo-like kinase, is transcriptionally repressed by p53 and induces apoptosis upon RNAi silencing. [2005]

These findings provide an attractive explanation for the crucial function of Plk4 in cell proliferation and have implications for the role of Polo kinases in tumorigenesis. [2005]

Plk4 is the most structurally divergent Polo family member; it is maximally expressed in actively dividing tissues and is essential for mouse embryonic development. [2005]

SAK [?] -/- mice die during embryogenesis, whereas SAK [?] +/- mice develop liver and lung tumors and SAK [?] +/- MEFs show mitotic abnormalities. [2005]

Transcriptional analysis with luciferase reporters driven by SAK promoter deletion fragments identified SP-1 and CREB binding sites, which together conferred a two-fold SAK repression by p53. [2005]

Biologically, SAK RNA interference (RNAi) silencing induced apoptosis, whereas SAK overexpression attenuated p53-induced apoptosis. [2005]

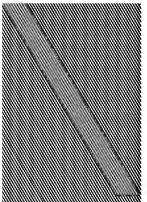
Computer search of a 1.7-kb SAK promoter sequence revealed three putative p53 binding sites, but p53 failed to bind to any of these sites, indicating that SAK repression by p53 was not through a direct p53 binding to the promoter. [2005]

Little has been, therefore, elucidated how Sak is regulated and how Sak contributes to cell proliferation. [2001]

SAK, a polo family member with unique properties, had not been systematically studied in any tumor type. [2001]

SAK and PLK are members of the polo family of serine [?] threonine [?] kinases, which in lower organisms have been shown to be required for the precise regulation of mitosis. [2001]

Functional validation using siRNA knockdown in multiple tumor cell lines showed that C13orf34, MAD2L1, PLK4, TPX2, and DSEPDC1B each significantly altered radiation sensitivity in at least two cancer cell lines. [2010]



This is achieved, in part, by an autoregulatory mechanism, whereby PLK4 autophosphorylates residues in a PEST sequence located carboxy-terminal to its catalytic domain. [2010]

We found that CUL1 is critical for the degradation of active PLK4 following deregulation of cyclin E/cyclin-dependent kinase 2 activity, as is frequently observed in human cancer cells, as well as for baseline PLK4 protein stability. [2009]

In addition, the formation of abnormal structures was abolished by expression of exogenous Plk4, but not SAS6 and Cep135/Bld10p, which are downstream regulators required for the organization of nine-triplet microtubules. [2009]

Sak serine-threonine kinase acts as an effector of Tec tyrosine [?] kinase. [2001]

RESULTS: In the majority of cases, both SAK and PLK were more highly expressed in tumor tissue than in adjacent normal intestinal mucosa. [2001]

Levels of SAK and PLK expression in tumor relative to paired normal mucosa correlated directly with patient age and with each other but did not correlate with tumor stage. [2001]

This phenotype depends on the presence of endogenous wild-type Plk4. [2010]

Plk4 [?] (+/-) murine embryonic fibroblasts (MEFs) at early passage show a high incidence of multinucleation, supernumerary centrosomes, and a near-tetraploid karyotype. [2010]

Sak [?] transcripts are present in S/G2/M phase cells, and in proliferating cell layers of the mouse embryo and adult tissues. [2000]

The Sak [?] gene encodes a serine [?]/threonine [?] kinase, which is a member of the Polo family of mitotic regulators. [2000]

top

Primer extension analysis of murine Sak [?] revealed one major transcription start site at position -303bp relative to the start of translation. [2000]

Using various Sak [?] promoter/luciferase constructs, the core promoter region required for expression was located within 400bp of the message Cap site, and sequence further 5' strongly suppressed transcription. [2000]

The murine Sak [?] gene is located on the proximal arm of mouse chromosome 13, as determined by RFLP analysis. [2000]

Plk4 [?] is required for cytokinesis and maintenance of chromosomal stability. [2010]

Here we show that loss of heterozygosity (LOH) occurs at the Plk4 [?] locus in 50% of human hepatocellular carcinomas (HCC) and is present even in preneoplastic cirrhotic liver nodules. [2010]

Our results indicate that haploid levels of Plk4 [?] disrupt RhoGTPase function during cytokinesis, resulting in aneuploidy and tumorigenesis, thus implicating early LOH at Plk4 [?] as one of the drivers of human hepatocellular carcinogenesis. [2010]

However when these cells commit to differentiate into trophoblast giant (TG) cells, Hand1 is **phosphorylated** by the polo-like kinase Plk4 (Sak) and released into the nucleus to activate downstream target genes. [2008]

In Drosophila, centrioles are not necessary for somatic cell divisions.(9,10) However, we show here that mitotic abnormalities arise in syncytial SAK/PLK4-derived mutant embryos resulting in lethality. [2008]

Polo-like kinase 4 [?] (Plk4 [?]) regulates both modes of centriole biogenesis, and Plk4 [?] deregulation has been linked to tumor development [1, 3]. [2011]

The conserved protein kinase Polo-like kinase 4 [?] (Plk4) has a key role in controlling centriole biogenesis. [2010]

ABSTRACT: Polo-like kinase 4 (PLK4) is a unique member of the Polo-like family of kinases that shares little homology with its siblings and has an essential role in centriole duplication. [2010]

We show that Plx4, the Xenopus homolog of mammalian Plk4 [?] and Drosophila Sak [?], induces de novo centriole formation in•vivo in activated oocytes and in egg extracts, but not in immature or in•vitro matured oocytes. [2011]

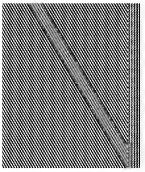
Moreover male meiosis fails in both SAK/PLK4 and DSAS-4 mutant spermatids that have no centrioles. [2008]

Here, we show that expression of stabilized mutant beta-catenin, which mimics mutations found in cancer, results in extra non-microtubule nucleating structures that contain a subset of centrosome proteins including gamma-tubulin and centrin, but not polo-like kinase 4 [?] (Plk4 [?]), SAS-6 or pericentrin. [2010]

One of these SSAPs was identified as Sak and was found in the virulent L. lactis phage ul36, which belongs to the Siphoviridae family [4, 5]. [2008]

In Staphylococcus aureus phages encoding immune evasion molecules (SAK, SCIN, CHIPS), which integrate specifically into the beta-haemolysin (Hlb) gene, are widely distributed. [2006]

The predicted protein sequences of Rab7a and Rab7b contain all characteristic domains essential for Rab function: the effector domain (YRATVGADF) and four GTP-binding consensus sequences (GDSGVGKT, WDTAGQ, NKLD, SAK) as well as the prenylation motif (-CC) at the C-terminus indispensable for Rab binding to the membrane. [2006]



Sea anemones have proven to be a rich source of pharmacological tools, and some of the SAK toxins are now useful drugs for the diagnosis and treatment of autoimmune diseases. [2009]